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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,964	07/17/2003	John Nicholas Staniforth	478.1063	2030

7590 12/11/2007

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/621,964	STANIFORTH ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51 and 69-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-51 and 69-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/17/07, 3/6/07
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed September 17, 2007 have been entered. Claims 1-51 and 69-73 are pending.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-51 and 69-73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9, 14-16, 98-100, and 125-126 of copending Application No. 10/413,022 ('022) in view of US 5,476,093 ('093) and Noakes (Journal of Aerosol Medicine, 1995 Spring; 8 Suppl 1:S3-7). Although the conflicting claims are not identical, they are not patentably distinct from

each other because '022 teaches the method of treating sexual dysfunction by inhaling apomorphine in the dosage and particle size herein claimed.

'022 does not expressly teach the use of pMDI with the herein claimed propellants and formulation. '022 does not expressly teach the use of dry powder inhaler that possess the herein recited characteristics.

Noakes teaches that the herein claimed propellants, HFA134a and HFA227, are commonly used to replace the already well-known CFC propellants.

'093 teaches a dry powder inhaler device that meets the herein claimed characteristics (See Fig. 3a for example).

It would have been obvious to one of ordinary skill in the art at the time of invention to employ the herein claimed inhaler or pMDI components in the '022's method of treating sexual dysfunction.

One of ordinary skill in the art would have been motivated to employ the herein claimed inhaler or pMDI components in the '022's method of treating sexual dysfunction as these agents and the use of dry powder inhaler are well-known in the inhalation medical technologies, and thus clearly within the purview of skilled artisan.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's remarks with regard to the outstanding double patenting rejection filed September 17, 2007 are acknowledged. In the mean time, the double patenting rejection remains.

Claim Rejections - 35 USC § 103

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims -51 and 69-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0006933 ('933) in view of US 5,699,789 ('789), Ensuring Patient Care, 2nd ed., 1999, pages 15-21, US 5,476,093 ('093), Lucas et al., (Pharmaceutical Research, 1999;16(10):1643-1647) and Noakes (Journal of Aerosol Medicine, 1995 Spring; 8 Suppl 1:S3-7.

'933 teaches a method of treating female sexual dysfunction and male erectile dysfunction by employing inhalation apomorphine (See paragraph 0031 – 0035, also

claims 6-7 and 12-16). '933 teaches the human sexual dysfunction and treatment thereof (See paragraph [0002] to [0010]). '933 also teaches the employment of adjunct agents such lactose (See paragraph 0055). '933 also teaches dry powder inhaler can be employed (See claim 7).

'933 does not expressly teach the dose of apomorphine. '933 does not expressly teach the particle size of the apomorphine. '933 does not expressly teach the use of the herein claimed force additives such as leucine. '933 does not expressly teach the use of a dry powder inhaler device possessing the herein claimed characteristics. '933 does not expressly teach the use of specific components such as CFC, HFA134a and HFA227.

'789 teaches the desirable particle size for inhalation delivery of drugs as 0.5-5 microns (see col. 2, line 4).

Ensuring Patient Care teaches also teaches the optimal particle size for the active as no more than 5-10 μm (See page 19, col. 2, fourth paragraph).

Noakes teaches that the herein claimed propellants, HFA134a and HFA227, are commonly used to replace the already well-known CFC propellants.

'093 teaches a dry powder inhaler device that meets the herein claimed characteristics (See Fig. 3a for example).

Lucas et al. teaches that leucine enhances the flow properties of the powders and improves the emptying of the device (See for example page 1646, col. 2).

It would have been obvious to one of ordinary skill in the art at the time of invention to employ the herein recited particle size and dosage of apomorphine in a

method of treating sexual dysfunction. It would have been obvious to one of ordinary skill in the art at the time of invention to employ the herein claimed ingredients into the inhalation formulation of apomorphine to treat sexual dysfunction.

One of ordinary skill in the art would have been motivated to employ the herein recited particle size and dosage of apomorphine in a method of treating sexual dysfunction. The optimal particle size for dry powder inhalation is known. Formulating apomorphine into such particle size would be reasonably expected to be effectively deliver apomorphine into the lung of the patients. Furthermore, according to '933, the therapeutic plasma concentration of apomorphine as about 5-10ng/ml. Therefore, the optimization of dosage range to herein claimed in order to achieve the optimal therapeutic plasma level of apomorphine is obvious as being within the skill of the artisan.

One of ordinary skill in the art would have been motivated to employ the herein claimed ingredients into the inhalation formulation of apomorphine to treat sexual dysfunction because I) the propellants such as CFC and HFA134a and HFA227 are well-known in the art to be used in pMDI aerosol formulation; II) leucine can improve the properties of the dry powder formulation and III) the dry powder inhalation device for delivering the drug is also known in the art. Therefore, employing these well-known agents and device for inhalation delivery of apomorphine to treat sexual dysfunction is considered obvious as being within the purview of the skilled artisan.

Response to Arguments

Applicant's arguments filed September 17, 2007 averring the cited prior art's failure to suggest or provide motivation to adjust the dosage to the herein claimed dosage have been fully considered but they are not persuasive. The inhalation route of administration is taught in '933, the dosage used in dog is taught in '933, and the therapeutic concentration for treating sexual dysfunction is also taught in '933. Therefore, based on the information provided in '933, one of ordinary skill in the art would have been motivated to adjust or optimize the dosage of inhalation apomorphine. As anyone of ordinary skill in the art will appreciate, there are many reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe infection would require a correspondingly higher dosage. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. For these and other self-evident reasons, it would have been obvious to have used much higher or lower dosages of apomorphine for inhalation to maximize the therapeutic effect and at the same time, minimize the side effect.

Applicant's arguments filed September 17, 2007 averring the teaching away of '933 have been considered, but are not found persuasive. Specifically, it is apparent that applicant believes '933 teaching apomorphine dosage for human being higher than that for dog. The examiner notes that in paragraph [0074] in '933 teaches the sub-lingual route of administration of apomorphine, not inhalation route of administration. It is not clear how 0.5mg of apomorphine would correspond to a dose of 3mg in human being. When considering the factors mentioned in the above paragraph: the route of

administration, animal dosage, and the therapeutic plasma concentration of apomorphine, one of ordinary skill in the art would be motivated to optimize the herein claimed dosage of apomorphine, absent evidence to the contrary.

Applicant's arguments filed September 17, 2007 averring the failure of '933 to teach the therapeutic plasma concentration have been considered, but are not found persuasive. The therapeutic concentration is taught in '933, the examiner notes that in the background section of '933, apomorphine is a well-known drug for treating sexual dysfunction. Although may be '933 is investigating the dosage of apomorphine to avoid or minimize side effect or apomorphine, let's not forget the therein claimed method is directed to the treatment of sexual dysfunction. Therefore, the targeted plasma concentration of apomorphine will be effective in treating sexual dysfunction, absent evidence to the contrary. Therefore, possessing the cited prior art's teachings, one of ordinary skill in the art would be motivated to optimize the herein dosage of apomorphine for the treatment of sexual dysfunction.

Applicant's arguments filed September 17, 2007 averring '933 teaches inhaling apomorphine would lead to inhaling large dose of lactose have been considered, but are not found persuasive. It is not clear why a large dose of lactose have to be used in formulating inhalation product. It may be true for oral formulation to include a large amount of filler (e.g. lactose) in the product. However, it may not be true that for inhalation product that a large amount of lactose will be used. The examiner would encourage the applicant to bring in evidence to show that a large amount of apomorphine is commonly used in inhalation product. Without such evidence,

applicant's arguments are not seen to be supported and therefore, the claims are still considered be properly rejected by the cited prior art.

Applicant's arguments filed September 17, 2007 averring '933's teachings away from the field of inhalation and toward intranasal or oral therapy have been considered, but are not found persuasive. The examiner notes that the inhalation method of apomorphine is recited in '933 (See claims 6 and 7).

Applicant's arguments filed September 17, 2007 averring '933's failure to teach the therapeutic effect in about nine minutes or less have been considered, but are not found persuasive. The examiner notes that there is no active method steps recited in the claims in order to for the therapeutic effect of sexual dysfunction method to be achieved in nine minutes or less. Therefore, such effect is considered to be inherently present in the method of '933.

Applicant's arguments filed September 17, 2007 averring the failure of '933 to teach dry powder formulation have been considered, but are not found persuasive. Claim 7 clearly claim the use of dry powder formulation for inhalation method of treating sexual dysfunction. The claims are considered properly rejected by the cited prior art.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617